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Correlation of T cell response and bacterial clearance in human volunteers challenged with Helicobacter pylori revealed by randomised controlled vaccination with Ty21a-based Salmonella vaccines

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Abstract

Background: Helicobacter pylori remains a global health hazard, and vaccination would be ideal for its control. Natural infection appears not to induce protective immunity. Thus, the feasibility of a vaccine for humans is doubtful. Methods: In two prospective, randomised, double-blind, controlled studies (Paul Ehrlich Institute application nos 0802/02 and 1097/01), live vaccines against H pylori were tested in human volunteers seronegative for, and without evidence of, active H pylori infection. Volunteers (n = 58) were immunised orally with Salmonella enterica serovar Typhi Ty21a expressing H pylori urease or HP0231, or solely with Ty21a, and then challenged with 2×105 cagPAI- H pylori. Adverse events, infection, humoral, cellular and mucosal immune response were monitored. Gastric biopsies were taken before and after vaccination, and postchallenge. Infection was terminated with antibiotics. Results: Vaccines were well tolerated. Challenge infection induced transient, mild to moderate dyspeptic symptoms, and histological and transcriptional changes in the mucosa known from chronic infection. Vaccines did not show satisfactory protection. However, 13 of 58 volunteers, 8 vaccinees and 5 controls, became breath test negative and either cleared Hpylori (5/13) completely or reduced the H pylori burden (8/13). H pylori-specific T helper cells were detected in 9 of these 13 (69%), but only in 6 of 45 (13%) breath test-positive volunteers (p = 0.0002; Fisher exact test). T cells were either vaccine induced or pre-existing, depending on the volunteer. Conclusion: Challenge infection offers a controlled model for vaccine testing. Importantly, it revealed evidence for T cell-mediated immunity against H pylori infection in humans.

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